

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C. 20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 25 July 2000 (25.07.00)	
International application No. PCT/US99/26824	Applicant's or agent's file reference 98,634-A
International filing date (day/month/year) 12 November 1999 (12.11.99)	Priority date (day/month/year) 12 November 1998 (12.11.98)
Applicant CARSON, Monica, J. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

06 June 2000 (06.06.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer F. Baechler Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

SEP 05 2000

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

10574

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

McDONNELL BOEHNNEN HULBERT
& BERGHOFF
Attn. ZIMMERMAN, ROGER, P.
300 South Wacker Drive,
32nd Floor
CHICAGO, IL 60606
UNITED STATES OF AMERICA

Date of mailing
(day/month/year)

29/08/2000

Applicant's or agent's file reference

98,634-A

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 99/26824

International filing date
(day/month/year)

12/11/1999

Applicant

DIGITAL GENE TECHNOLOGIES, INC. et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Véronique Baillou

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

DOCKETED

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

JUL 07 2000

To:

ZIMMERMAN, ROGER, P.
McDONNELL BOEHNNEN HULBERT
& BERGHOFF
300 South Wacker Drive,
32nd Floor
CHICAGO, IL 60606
ETATS-UNIS D'AMERIQUE

DATE

BY: *MB CP*

NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing
(day/month/year)

28.06.00

Applicant's or agent's file reference
98,634-A

IMPORTANT NOTIFICATION

International application No.

PCT/US 99/ 26824

International filing date (day/month/year)

12/11/1999

Priority date (day/month/year)

12/11/1998

Applicant

DIGITAL GENE TECHNOLOGIES, INC. et al.

1. The applicant is hereby **notified** that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

06/06/2000

2. This date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- ☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- ☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA:

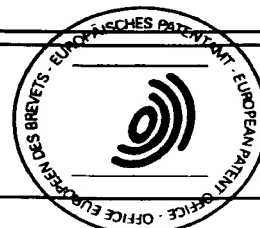


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Authorized officer

KENNEDY M B

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PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ZIMMERMAN, ROGER, P.
McDONNELL BOEHNEN HULBERT
& BERGHOFF
300 South Wacker Drive,
32nd Floor
CHICAGO, IL 60606
ETATS-UNIS D'AMERIQUE

12/19/00
AB [Signature]

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing (day/month/year) 19.09.2000	
Applicant's or agent's file reference 98,634-A	REPLY DUE within 3 month(s) from the above date of mailing
International application No. PCT/US99/26824	International filing date (day/month/year) 12/11/1999
Priority date (day/month/year) 12/11/1998	
International Patent Classification (IPC) or both national classification and IPC C12N15/00	
Applicant DIGITAL GENE TECHNOLOGIES, INC. et al.	

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain document cited
 - VII ☒ Certain defects in the international application
 - VIII ☒ Certain observations on the international application
3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 12/03/2001.

Name and mailing address of the international preliminary examining authority:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized officer / Examiner

Muller-Thomalla, K

Formalities officer (incl. extension of time limits)

Sinanovic, E

Telephone No. +31 70 340 2672



WRITTEN OPINION

International application No. PCT/US99/26824

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-109 as originally filed

Claims, No.:

1-54 as originally filed

Drawings, sheets:

1/17-17/17 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. Part of claims 1-10,17,18,29,30 and whole of claims 11-16,19-28,31-54,

because:

- ☒ the said international application, or the said claims Nos. 17,18 relate to the following subject matter which does not require an international preliminary examination (*specify*):

WRITTEN OPINION

International application No. PCT/US99/26824

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. Part of claims 1-10,17,18,29,30 and whole of claims 11-16,19-28,31-54.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-10,17,18,29,30
Inventive step (IS)	Claims
Industrial applicability (IA)	Claims 17?,18?

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

ad section III

Claims 17 and 18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

ad section V

The following documents D1 to D4 cited in the International Search Report are referred to in this opinion. The respective numbering of said documents corresponds to their order of appearance in said Search Report. See in particular those passages cited as relevant in said Search Report.

1. Due to the lack of an indication of the fragment length of the claimed polynucleotide in claim 1 and due to the lack of any indication of the origin or specificity of the claimed nucleotide, any polynucleotide fragment of the prior art will take away the novelty of present claims 1-6 (in this respect see D1, D2 and D4 cited in the present Search report).
2. The prior art is replete with recombinant vectors comprising nucleic acids and methods for producing the same. Claims 7-10 thus also lack novelty. The same objection is valid for the treatment and diagnostic method of claims 17 and 18 and the kit and method of claims 29 and 30. It should be noted that the latter claims are not limited to polynucleotides or their use with at least 10 contiguous bases of Seq. No1 (invention I).
All of the claims 1-10, 17, 18, 29, 30 of invention thus lack novelty under the requirements of Article 33(2) PCT.
3. For the assessment of the present claims 17 and 18 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however,

claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

ad section VII

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D4 are not mentioned in the description, nor are these documents identified therein.
2. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the Applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT).

If the Applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

ad section VIII

1. As already highlighted in the International Search Report, all of features b) to c) are considered to render the scope of claim 1 and the claims related thereto indefinite and unclear (Article 6 PCT). The same objection is valid for the feature "fragment" in feature a) of claim 1.
2. Method claim 8 does not contain a single method step (Article 6 PCT).
3. The vague and imprecise statement in the description on page 81, lines 5-8 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

ZIMMERMAN, ROGER, P.
McDONNELL BOEHNEN HULBERT
& BERGHOFF
300 South Wacker Drive,
32nd Floor
CHICAGO, IL 60606
ETATS-UNIS D'AMERIQUE

PCT

AB / 4m3

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year) 19.02.2001

Applicant's or agent's file reference
98,634-A

IMPORTANT NOTIFICATION

International application No.
PCT/US99/26824

International filing date (day/month/year)
12/11/1999

Priority date (day/month/year)
12/11/1998

Applicant
DIGITAL GENE TECHNOLOGIES, INC. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office - P.B. 5818 Patentlaan 2
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Fax: +31 70 340 - 3016

Authorized officer

Sinanovic, E

Tel. +31 70 340-2672



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 98,634-A	<div style="display: flex; justify-content: space-between;"> <div> FOR FURTHER ACTION </div> <div> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) </div> </div>	
International application No. PCT/US99/26824	International filing date (<i>day/month/year</i>) 12/11/1999	Priority date (<i>day/month/year</i>) 12/11/1998
International Patent Classification (IPC) or national classification and IPC C12N15/00		
Applicant DIGITAL GENE TECHNOLOGIES, INC. et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 16 sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 06/06/2000	Date of completion of this report 19.02.2001	
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016 </div> </div>	Authorized officer Muller-Thomalla, K Telephone No. +31 70 340 4230	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US99/26824

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

4-80,82-100, as originally filed
102-109

1-3,81,101 as received on 18/12/2000 with letter of 18/12/2000

Claims, No.:

1-91 as received on 18/12/2000 with letter of 18/12/2000

Drawings, sheets:

1/17-17/17 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US99/26824

☒ claims Nos. Part of claims 1,3,10-14,25,26,31,41,42,67,68 and whole of claims 2,4-9,15-24,27-30,32-40,43-66,69-91 .

because:

☒ the said international application, or the said claims Nos. 25,26,67,68 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. Part of claims 1,3,10-14,25,26,31,41,42,67,68 and whole of claims 2,4-9,15-24,27-30,32-40,43-66,69-91.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1,3,10-14,25,26,31,41,42,67 and 68
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1,3,10-14,25,26,31,41,42,67 and 68
Industrial applicability (IA)	Yes:	Claims	1,3,10-14,31,41,42
	No:	Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US99/26824

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/26824

ad section I

Sequence listing pages 1-14 filed with the letter of 12.11.1999 do not form part of the application (Rule 13^{ter}.1(f) PCT) and will not be annexed to this report.

ad section III

Claims 25,26,67 and 68 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

ad section V

1. The following documents D1 and D2 cited in the International Search Report are referred to in this Report.

D1 : THAKKER-VARIA S ET AL: "Gene expression in activated brain microglia: identification of a proteinase inhibitor that increase microglial cell number." BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (1998 MAY) 56 (1-2) 99-107., XP000886332

D2: CARSON, M. J. (1) ET AL: "Characterization of microglial-specific gene expression." SOCIETY FOR NEUROSCIENCE ABSTRACTS, (1998) VOL. 24, NO. 1-2, PP. 1614. MEETING INFO.: 28TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PART LOS ANGELES, CALIFORNIA, USA NOVEMBER 7-12, 1998, XP000886325

See in particular those passages cited as relevant in said Search Report.

The Applicant replaced the original 54 claims by 91 amended claims.
As already made clear in the Search Report, only those parts of the multiple (35) inventions and those parts of the claims which are clear and contain defined searchable features have been searched.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/26824

Consequently, in this case the only invention examined in the IPER relates to invention I (first invention of the 35 identified inventions) as searched, which relates to nucleic acid sequence No. 1 comprising at least 95% sequence identity with the sequence as defined in seq. No. 1 and which relates to clearly defined subject-matter (with a clear support in the description and examples) related thereto (fragments, antibodies etc. excluded...see International Search Report). Attention is thus again drawn to the clarity objections underlying the lack of establishment of the search report formulated in the International Search Report for the present application.

Thus the only new 14 claims examined (only partly examined: for reasons please see International Search Report) are the following:

Claims 1,3,10,11-14,25,26,31,41,42,67 and 68 which partly correspond to original claims 1,4,7-10,18 and 30. The remaining former 6 claims previously examined have either been deleted by the Applicant or reformulated in such a way that they fall under the category "unsearched claims" for the reasons mentioned in the Search Report.

2. In the light of the restriction of the subject-matter of claimed invention I (only invention searched) to a sequence with a sequence identity of least 95% with sequence No. 1 (only sequence searched), the subject-matter of the present claimed subject-matter appears to be novel in the light of the cited documents D1 and D2.
3. The claimed subject-matter of the claims of invention I does, however, not appear to satisfy the requirements of Article 33(3) PCT for lack of inventive step in the light of D1 and D2.
 - 3.1 According to the present description (see e.g. page 6 onwards) the problem to be solved by present invention I is the definition of patterns of gene expression that would distinguish normal or resting microglia from activated microglia. According to page 6, last paragraph. "such patterns could be determined, for example, by identifying gene expression regulated by the inflammatory response (e.g. LPS/IFNgamma stimulation)....such a systematic characterisation would allow the identification of harmful molecules that contribute to the neuroinflammatory pathologies associated with neurodegenerative conditions".

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/26824

Prior art Document D1 describes such gene expression in LPS-activated brain microglia, whereby the profile of gene expression is compared to that in basal control cultures. Said document thus solves the same problem as for the present invention I. The same reasoning is valid for cited document D2 which specifically mentions the following:

"....it has been difficult to discern the relative contribution of microglia vs infiltrating macrophage towards neurodegeneration vs neuroprotection. Here we use a PCR-based gene expression assay TOGA (Total Gene expression Analysis) to characterize mRNA expressed by microglia and macrophage so as to recognize activation-specific and cell type-specific gene expression that would distinguish microglia from infiltrating macrophage".

According to the Applicant, document D1 does not disclose any specific nucleotide sequences in this respect and novelty of the present sequence No. 1 can indeed therefore be acknowledged for the specifically defined sequence No. 1.

- 3.2 However, although neither D1 or D2 explicitly disclose the specific sequence of the present polynucleotide sequence No. 1, they nevertheless suggest methods for finding such sequences in addition to those partially disclosed in said documents. It thus appears that the present polynucleotide sequence No. 1 represents a mere alternative to those already partly known, and considering that only known standard methods were used to discover the present disclosed sequence, no inventive skill was required from the skilled person. It would rather appear that routine experimentation would have lead to the present claimed sequence.
- 3.3 The remaining claims related to present claim 1 do not contain any further features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.
4. For the assessment of the present claims 25,26,67 and 68 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/26824

the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

ad section VIII

Method claim 13 does not contain a single method step (Article 6 PCT).